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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

CORCEPT THERAPEUTICS, INC., ***Plaintiff,*** **v.** **TEVA PHARMACEUTICALS USA, INC.,** ***Defendant.***	Civil Action No. 1:18-cv-03632 (RMB)(LDW) *Filed Electronically* **CONTAINS CONFIDENTIAL INFORMATION** **FILED UNDER SEAL**

TEVA'S POST-TRIAL BRIEF

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To show induced infringement, Corcept has the burden of proving that (i) people will use Teva's generic product to directly infringe the claimed methods and (ii) Teva has specific intent to induce such infringement. Corcept has failed to prove either element.

Corcept has failed to show even a single instance of anyone practicing the asserted claims. Yet it asks the Court to conclude that Teva's label is likely to encourage clinicians to practice the claims when the materially identical Korlym label has not. The Court should decline that invitation. Given the difficulties of dosing mifepristone, physicians would avoid using it in combination with a strong CYP3A inhibitor, particularly with the introduction of newer alternative drugs. And, even if one were to co-administer the two drugs, following Teva's label will not inevitably lead one to infringe: the label includes non-infringing dose options as well as infringing ones. Corcept has thus failed to meet its burden.

Corcept has also failed to demonstrate specific intent. Each asserted claim requires co-administering mifepristone and a strong CYP3A inhibitor to a Cushing's syndrome patient. But Teva's label does not encourage co-administration. Instead, the label warns *against* it because doing so can increase blood plasma levels of mifepristone. To be sure, the label provides instructions about *how* to co-administer if the physician, based on his or her independent medical judgment, decides to do so notwithstanding the risks. But, as a matter of law, that is not active inducement. The Federal Circuit has squarely held that instructions in the form "if you do X, then do Y" do *not* amount to instructions to do X in the first place. *HZNP Meds. LLC v. Actavis Lab'ys UT, Inc.*, 940 F.3d 680, 702 (Fed. Cir. 2019). That is precisely the form the instructions in Teva's label take: they specify "adjustment[s] to dose of mifepristone tablets *if adding a strong CYP3A inhibitor*." JTX-011.4 (emphasis added). Corcept does not and cannot point to *anything* in Teva's label that encourages co-administration in the first instance.

I. Corcept has failed to establish a likelihood of direct infringement.

Infringement can happen only in three specific ways: (a) start mifepristone at 1200 mg, lower the dose to 900 mg or 600 mg and add a strong CYP3A inhibitor (claim 10 of the '214 patent and claim 1 of the '800 patent); (b) start mifepristone at 900 mg, lower the dose to 600 mg, and add a strong CYP3A inhibitor (claim 1 of the '214 patent); or (c) start with a strong CYP3A inhibitor and then add mifepristone at a dose of 900 mg (claim 6 of the '800 patent).[1]

A. There is no evidence that anyone has ever practiced the asserted claims.

Corcept failed to introduce evidence that anyone has ever practiced any asserted claim. The two experts who testified live—Dr. Snyder and Dr. Carroll—have never prescribed the two drugs together, much less at the claimed doses and in the claimed order. Tr. 266:9–12, 266:18–23, 273:17–19 (Carroll); Tr. 410:9–22 (Snyder). Dr. Carroll could not identify any specific instances of infringement. Tr. 270:20–23 (Carroll). Nor could Dr. Synder. Tr. 392:7–393:3 (Synder). Corcept's Senior Medical Director has never co-administered the two drugs and is not aware of any physicians who have. Tr. 96:18–23; 97:23–98:15 (Moraitis).

Corcept introduced evidence only of occasional co-administration *at noninfringing doses*: *First*, Dr. Dobs has treated about a hundred Cushing's patients but co-administered mifepristone and ketoconazole only "two to three times." Tr. 51:24–52:8; 58:16–21. But Corcept has no evidence of the order of administration, the doses used, or any dose adjustment. *Second*, Dr.

[1] At trial, Corcept argued that claim 6 of the '800 patent required only "one active step" of administering 900 mg mifepristone to a patient taking a strong CYP3A inhibitor. Tr. 225:3–5 (Carroll); *see* Tr. 477:21–23. It is not clear what Corcept means by this. What matters is that—as the Court observed, *e.g.*, Tr. 481:17–21 and 483:5–14—the claim requires the physician to give mifepristone to a patient already taking a strong CYP3A inhibitor, that is, co-administer the drugs. This construction is consistent with the claim language, prosecution history, and Dr. Belanoff's testimony. The whole point of the patents was Corcept's allegedly surprising discovery that one could *co-administer mifepristone and strong CYP3A inhibitors* at higher doses than previously thought possible. *See, e.g.*, Tr. 13:18–21 (Opening), 127:17–155:21 (Belanoff).

Carroll relied on hearsay from Corcept's expert Dr. Hamrahian, who stated that he co-administered a strong CYP3A inhibitor with mifepristone. Tr. 285:2–5. But Dr. Carroll did not know what dose of mifepristone or which CYP3A inhibitor were used or whether Dr. Hamrahian practiced the asserted claims. Tr. 285:10–19. *Third*, Dr. Carroll relied on two case reports but admitted that neither discloses infringement. *See* Tr. 282:18–283:6 (400 mg mifepristone with ketoconazole does not infringe); Tr. 276:9–13 (300 mg mifepristone with ketoconazole does not infringe). *Finally*, Corcept asked questions about a 2019 case report entitled "Failure of Medical Therapy to Control [sic] Hypercortisolemia," Tr. 490:9–10 (Snyder), in which mifepristone and ketoconazole were administered to a patient who later died. Tr. 461:19–23, 463:8–10 (Snyder). The paper did not report the dose of mifepristone administered. Tr. 463:22–25 (Corcept's counsel's confirmation to Court). Thus, Corcept has failed to show past infringement.

B. Corcept has failed to show future direct infringement.

While "a patentee does not need to prove an actual past instance of direct infringement by a physician to establish infringement in an ANDA case . . . past conduct is relevant to what will happen in the future." *Genentech, Inc. v. Sandoz Inc.*, 55 F.4th 1368, 1379 (Fed. Cir. 2022) (quoting *Vanda Pharms. Inc. v. W.-Ward Pharms. Int'l Ltd.*, 887 F.3d 1117, 1129–30 (Fed. Cir. 2018)). "Determining what will . . . happen when a product enters the market requires 'consideration of all the relevant evidence,' including the proposed label's instructions and physician practice." *Id.* (citation omitted). Here, even co-administration—let alone co-administration at the claimed doses and in the claimed order—is exceedingly unlikely because: (1) mifepristone is difficult to dose correctly, so physicians would not want to add another drug that increases mifepristone blood levels; (2) newer and easier-to-dose drugs, such as osiliodrostat, are now available; and (3) Teva's label warns against co-administration.

1. A physician would not co-administer mifepristone and a strong CYP3A inhibitor given the difficulty of dosing mifepristone.

Mifepristone does not decrease cortisol levels but rather blocks the action of cortisol on the body. Tr. 159:14–22 (Belanoff); Tr. 384:24–385:1 (Synder). So a physician administering mifepristone cannot measure cortisol or ACTH to determine the proper dose. Tr. 159:18–160:3 (Belanoff); Tr. 385:16–20 (Snyder) ("[T]he major drawback is that because it doesn't block the production of cortisol, one cannot use cortisol to determine if one is giving the right dose. So one doesn't know if one's giving the right dose or too much or too little."). Strong CYP3A inhibitors raise mifepristone blood levels and therefore increase the chances of dangerous side effects that could result in death. Tr. 303:9–22 (Carroll). A dose of mifepristone that is safe and effective when given alone can decrease the activity levels of cortisol to a dangerous degree when co-administered with a strong CYP3A inhibitor. Tr. 303:14–22 (Carroll).

Co-administration of mifepristone and ketoconazole presents particular risks. Corcept's medical director testified that he would not use ketoconazole to treat Cushing's because the drug suffers from many problems, including liver toxicity, inhibition of gonadal hormone production, cardiotoxic effects, and potential hypokalemia. Tr. 93:4–96:17 (Moraitis). With the approval of other drugs for Cushing's, Dr. Moraitis thought a physician would not select ketoconazole. Tr. 100:1–4. Dr. Moraitis also testified that he prefers monotherapy and that, "when you have to use two agents, then you're in big trouble." Tr. 96:24–97:7.

2. The introduction of osilodrostat makes co-administration obsolete.

The introduction of newer Cushing's drugs such as osilodrostat obviates any need to co-administer mifepristone and strong CYP3A inhibitors. Tr. 393:11–18 (Snyder). Osilodrostat is a powerful and effective drug that acts quickly. Tr. 386:19–22 (Snyder). Unlike mifepristone, osilodrostat inhibits the synthesis of cortisol, so a physician can easily determine the proper dose

of osilodrostat by measuring cortisol levels. Tr. 384:9-12, 386:17–19 (Snyder).

Corcept may argue that there are two reasons osilodrostat would not replace mifepristone for a patient who needs a strong CYP3A inhibitor: (1) osilodrostat is indicated for Cushing's Disease—a narrower indication than Cushing's syndrome—and (2) the label for osilodrostat recommends reducing the dose by half when co-administering with strong CYP3A inhibitors, suggesting it is less safe than mifepristone. But neither concern holds any weight. As to the first, Dr. Snyder explained that "FDA approval [of osilodrostat and Korlym] doesn't overlap," but it is "desirable to use osilodrostat for any form of Cushing's syndrome, and preferable to use it compared to mifepristone." Tr. 476:21–24 (Snyder). As to the second point, it is safer to administer osilodrostat than mifepristone with a strong CYP3A inhibitor because, with osilodrostat, a physician can measure cortisol levels to determine whether the correct dose of the drug is being administered. Tr. 489:10-20 (Snyder).

3. Teva's label warns against co-administration.

Finally, Teva's label warns against co-administration of mifepristone and a strong CYP3A inhibitor. Tr. 393:11–18 (Snyder). Section 2.5 states that the drugs should be used in combination only when necessary, as blood concentration of mifepristone can rise. Tr. 394:18–395:8, 399:412 (Snyder discussing JTX-011.4). Sections 5.6 and 7.2 of the label contain warnings against co-administration. Tr. 396:14–18 (Snyder). The medication guide, the portion of the label directed to patients, also contains warnings, and tells patients there could be strong side effects when mifepristone is given with other drugs like strong CYP3A inhibitors. Tr. 397:7–16 (Snyder). Dr. Snyder testified that, taken as a whole, "the label says to the physician, be scared. Be very scared. This could cause a problem." Tr. 397:17–22.

C. Corcept's arguments on direct infringement are unavailing.

In support of direct infringement, Corcept relies heavily on FDA's 2012 statements during the approval of Korlym that there was a potential for co-administration of mifepristone and ketoconazole. But the evidence has shown that the FDA's prediction was simply wrong. Eleven years later, cases of co-administration are rare, and cases of infringement are nonexistent.

Corcept's argument that direct infringement can be inferred from the label is also unavailing. As discussed below, the label does not recommend co-administering at all. And as Dr. Carroll testified, a physician can co-administer the two drugs, faithfully follow the instructions on the label, and not infringe the claims—for example, by administering 300 mg mifepristone to a patient taking a strong CYP3A inhibitor. Tr. 267:10–13, 268:5–12 (Carroll). Corcept has failed to adduce any evidence that one would follow the label's purportedly infringing instructions rather than the non-infringing instructions. Especially given the lack of evidence of any past infringement, the presence of non-infringing options on the label is significant and fatal to Corcept's case.

Takeda Pharms. U.S.A., Inc. v. W.-Ward Pharm. Corp., 785 F.3d 625 (Fed. Cir. 2015) is instructive. There, three drug-drug interaction ("DDI") patents disclosed methods for preventing gout flares by co-administering a reduced dose of colchicine with other drugs. *Id.* at 627. The district court held that Takeda did not show direct infringement, and the Federal Circuit affirmed. *Id.* at 634–35. The Federal Circuit's decision rested on two key findings: (1) there was no evidence that anyone had practiced the claimed methods; and (2) the generic's product "would not likely be used to directly infringe." *Id.* at 634. As to the latter, the Federal Circuit affirmed that co-administration was not likely due to a "narrow" "margin between an effective dose and a toxic dose [of colchicine]" and expert testimony that clinicians could "try to and can easily avoid concomitant administration of the drugs." *Id.* at 635. And, even if a clinician decided to co-

administer, a clinician could follow the label's instructions on how to dose colchicine if co-administered with one of the specified drug inhibitors without ever infringing the DDI patents. *Id.* The same is true here: there is no evidence of past infringement; the evidence shows that physicians would try to avoid co-administration of mifepristone and strong CYP3A inhibitors; and even if a physician decided to co-administer, he or she could do so according to the label without infringing. Accordingly, there is no evidence supporting future infringement.

In addition, claims 10–13 of the '214 patent and claim 1 of the '800 patent require that the patient start on an initial dose of either 900 mg or 1200 mg before the dose is lowered and a strong CYP3A inhibitor is added. Corcept has failed to show that many—indeed, any—patients take these doses and then reduce them. Corcept's Chief Commercial Officer, Mr. Maduck, has no information about the number of patients who previously received 1200 or 900 mg of Korlym, were prescribed a strong CYP3A inhibitor, and then reduced the mifepristone dose. Tr. 82:10–14. Corcept does not know the average dose that each patient received, Tr. 83:19–21, or the number of patients (if any) being prescribed Korlym who are also taking ketoconazole. Tr. 81:19–82:3 (Maduck).

In an effort to backfill Corcept's case, Corcept elicited testimony from Dr. Carroll on redirect that "most" patients taking only mifepristone require more than 900 mg to achieve efficacy. To the extent the Court permits this testimony, it is insufficient to show direct infringement.[2] Dr. Carroll's assertions on this score rely not on his own clinical experience but rather his memory of a 14-year-old study (the SEISMIC study) that led to the approval of

[2] In his reports, Dr. Carroll did not opine on the results of the SEISMIC study or the average dosage required for efficacy. This undisclosed expert testimony is the subject of a motion to strike on which the Court reserved. Tr. 323:15–19; *see also* Tr. 321:4–322:19, 327:19–23. To the extent Corcept characterizes this as fact testimony, Dr. Carroll is not listed as a fact witness in the Pretrial Order.

Korlym (and that Corcept did not introduce into evidence). Tr. 332:15–24 (Carroll). Only 34 participants completed this non-placebo-controlled study. Tr. 333:6–9 (Carroll). That trial did not involve co-administration of mifepristone with any strong CYP3A inhibitor, so it tells nothing about the likelihood of infringement. Tr. 333:14–16 (Carroll).

Corcept contends that infringement of claim 6 of the '800 patent is likely because a physician need only prescribe a dosage of 900 mg mifepristone to a patient on a strong CYP3A inhibitor to infringe. But the physician must still make the decision to co-administer in the first place, which is unlikely for the reasons explained above. Corcept also ignores the language in the label requiring starting at 300 mg and then slowly titrating upward only if clinically necessary. A dosage of mifepristone under 900 mg would not infringe claim 6, and Corcept has failed to introduce any evidence that a physician would titrate the dose all the way 900 mg. Indeed, the evidence suggests the opposite: Corcept has not introduced any evidence of co-administration of a strong CYP3A inhibitor and mifepristone at a dose higher than 400 mg.

D. *Genentech* dismantles Corcept's infringement case.

The Federal Circuit's decision in *Genentech* illustrates the problems with Corcept's case. There, two DDI patents recited methods of co-administering pirfenidone and fluvoxamine or other strong CYP1A2 inhibitors, 55 F.4th at 1375–76. Sandoz's label warned of potential DDI's associated with co-administering those drugs, but it provided instructions on how to dose pirfenidone when necessary to co-administer the two agents. The Federal Circuit affirmed the district court's finding of no direct infringement for two main reasons. First, there was no evidence that any physician had ever co-administered pirfenidone and fluvoxamine at an infringing dose, and "past conduct is relevant to what will happen in the future." *Id.* at 1379. Second, Sandoz presented testimony from physicians that they would likely avoid co-administering the two drugs and choose a non-infringing treatment instead. *Id.* at 1380. The same

result should follow in this case. Corcept has failed to show any instance of direct infringement, and Dr. Synder testified physicians would avoid co-administering the two drugs together. Thus, Corcept fails to meet its burden on direct infringement.

The Federal Circuit also considered—and rejected—Genentech's argument that "the DDI instructions must be important because the FDA insisted on including them in the label." *Id.* "Even if the FDA had been concerned about the possibility that a patient may be treated with both pirfenidone and fluvoxamine," the court explained, "that does not establish by a preponderance of the evidence that if Sandoz's drug were put on the market, it would infringe the asserted DDI claims." *Id.* (cleaned up). The same is true here: even if FDA was concerned about the possibility of co-administration *in 2012*, that is insufficient to establish that if Teva's drug were put on the market *today*, it would lead to infringement.[3]

II. Teva will not induce infringement as a matter of law.

"To prove inducement, a plaintiff must present evidence of active steps taken to encourage direct infringement; mere knowledge about a product's characteristics or that it may be put to infringing uses is not enough." *HZNP*, 940 F.3d at 701 (citing *Takeda*, 785 F.3d at 630–31). In the ANDA context, the inducement inquiry focuses on whether the generic's label "encourage[s], recommend[s], or promote[s] infringement." *Id.* at 701–02. Here, the answer to that question is plainly no. Teva's label does not encourage co-administration of mifepristone and strong CYP3A inhibitors. Quite the contrary; the label cautions against doing so because of

[3] In contrast, in all of the cases upon which Corcept relies, the patentee showed past infringement, making an inference of future infringement justified. *Janssen Pharms., Inc. v. Mylan Lab'ys Ltd.*, No. 20cv13103 (EP) (LDW), 2023 WL 3605733, at *7, *17, *25 (D.N.J. May 23, 2023) (more than 50% of patients miss a dose; resulting reinitiation of therapy infringes); *Vanda,* 887 F.3d at 1130 (testifying expert practiced the claims); *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1046, 1058 (Fed Cir. 2010) (undisputed evidence of past infringing use).

the associated risks while offering advice about *how* co-administration should be performed *if* the physician decides to do it despite the warnings. But an instruction *how* to do something is not an instruction *whether* to do it in the first place. The latter is inducement; the former is not. *See HZNP*, 940 F.3d at 702. Corcept's inducement case fails as a matter of law.

A. Teva's label does not actively induce performance of the patented methods.

1. Teva's label does not encourage co-administration of a strong CYP3A inhibitor with mifepristone, as required by all asserted claims.

Each asserted claim requires that a physician co-administer mifepristone with a strong CYP3A inhibitor. Teva's label nowhere recommends such co-administration. *See* Tr. 483:22–484:4 (Snyder). Instead, the label describes what a physician should do *if* he or she decides on that course of action. Tr. 488:14–18 (Snyder); *see also* Tr. 349:11, 13–16 ("THE COURT: … [W]hether or not to co-administer these drugs is a discretionary call on the part of the physician, is it not? MR. CERRITO: As much so as any drug, yes.").

Table 1 of Teva's label is explicit on this point: "Adjustment to dose of mifepristone tablets *if adding a strong CYP3A inhibitor*." JTX-011.4 (emphasis added). Under black-letter law, that is insufficient to show inducement: "Merely describing the infringing use"—as opposed to affirmatively recommending it—is not enough. *HZNP*, 940 F.3d at 702. If anything, Teva's label cautions against co-administration of strong CYP3A inhibitors with mifepristone. *See* Tr. 394:9–11 (Snyder) ("[Q.] [A]t a high level, what does Teva's label say about co-administering mifepristone and strong CYP3A inhibitors? A. It says be afraid. Be very afraid."); Tr. 399:9–12 (Snyder) (similar). Section 2.5 notes that "strong inhibitors of CYP3A … may increase exposure to mifepristone" and instructs that "[m]ifepristone tablets should be used in combination with strong CYP3A inhibitors only when necessary." JTX-011.4; *see* Tr. 394:18–395:8 (Snyder).

The "Warnings and Precautions" and "Drug-Drug Interactions" sections of the label have similar warnings. *See* JTX-011.5–6, .13 ("Mifepristone should be used with caution in patients taking ketoconazole and other strong inhibitors of CYP3A … as these could increase the concentration of mifepristone in the blood. The benefit of concomitant use of these agents should be carefully weighed against the potential risks. Mifepristone should be used in combination with strong CYP3A inhibitors only when necessary, and in such cases the dose should be limited to 900 mg per day."); JTX-011.9, .13 (similar); Tr. 396:2–18, 397:17–22 (Snyder). During prosecution of the '214 patent, Corcept characterized nearly identical language in the 2012 Korlym label as teaching physicians "to avoid use of mifepristone with CYP3A inhibitors," JTX-005.707, and as "contraindicat[ing]" the combination, JTX-005.1014. Corcept's own arguments thus show that, far from encouraging co-administration, the label warns against it.

There are, to be sure, differences between the 2012 label and the current label. Tr. 215:2–11 (Carroll) (describing differences). For example, the 2012 label's recommendation of "extreme caution" when co-administering has been revised to "caution," and the allowed dose of mifepristone has been raised from 300 to 900 mg. *See id.* But it is not credible for Corcept to suggest that these changes transmuted the relevant passages from active *discouragement* to active *encouragement*. The far more reasonable conclusion is that the "forceful[]" warning against co-administration in the 2012 label, JTX-005.682, Tr. 169:24–170:6, 178:3–9, 182:19–20 (Belanoff), was revised to a less forceful warning—but still a warning nonetheless. *Cf.* Tr. 287:8–15 (Carroll) (admitting "there are still risks associated with the co-administration of mifepristone and strong CYP3A inhibitors"). A warning about the consequences of doing something is not the same as an instruction to do that thing. *See Otsuka Pharm. Co., Ltd. v. Torrent Pharms. Ltd., Inc.*, 99 F. Supp. 3d 461, 490 (D.N.J. 2015) ("incidental references to even

infringing uses in [the warnings] sections" of a label are "insufficient to constitute … encouragement, as opposed to mere permission" and cannot serve "as a basis for inducement liability"); *United Therapeutics Corp. v. Sandoz, Inc.*, No. 12-CV-01617, 13-CV-316, 2014 WL 4259153, at *18 (D.N.J. Aug. 29, 2014) ("[T]here is a rather significant difference between a warning and an instruction. A warning provides information regarding a potential risk. It does not prescribe a course of action.").

Table 3 in the label does not alter the analysis. It contains a summary of the results of various drug-drug interaction studies that Corcept ran in healthy patients. *See* JTX-011.14. It tells physicians the amount by which co-administration of strong CYP3A inhibitors with mifepristone increased mifepristone blood concentration in those studies, and it states that a dose adjustment of mifepristone is required if mifepristone is co-administered with strong CYP3A inhibitors. *See* Tr. 443:12–21 (Snyder). But, as Dr. Snyder explained, neither Table 3 nor anything else in the label contains anything that would encourage physicians to give the two drugs together in the first place. *See* Tr. 402:9–405:10. It neither identifies any situation in which co-administration would be desirable nor describes any benefits associated with it. Tr. 399:20–22, 402:9–12, 409:9–12, 410:1–3 (Snyder). Dr. Carroll admitted this. *See* Tr. 299:12–300:2.

In short, while Teva's label *describes* infringing uses—in the form of dosing recommendations to physicians who choose to co-administer mifepristone and strong CYP3A inhibitors—it does not encourage them. And it is black-letter law that "[m]erely describing the infringing use, or knowing of the possibility of infringement, will not suffice [for liability]; specific intent and action to induce infringement must be shown." *HZNP*, 940 F.3d at 702.[4]

[4] Throughout this case, Corcept has ignored the requirement that the label encourage co-administration. Instead, Corcept simply assumes co-administration will happen and focuses on the fact that, *if it does*, the label recommends infringing dose adjustments (as well as non-

Critically, Dr. Carroll failed to appreciate this point. In his understanding, merely *describing* a patented method is sufficient for infringement. Tr. 318:13–17. And mere descriptions of infringement are all Dr. Carroll identified. When asked by his counsel "[w]hat instructions in the [sic] Teva's label encourage you whether to co-administer mifepristone with a strong CYP3A inhibitor in the first instance," Dr. Carroll replied that "the label as a whole *talks about this co-administration*. It gives specific instructions on *how to administer these doses*." Tr. 328:13–18 (emphases added); *see also* Tr. 329:7–330:8 (similar). Dr. Carroll did not identify any portions of the label that actually recommend co-administration. That is because there are none.

2. Teva's product has substantial non-infringing uses.

As explained in Section I above, Teva's product has substantial non-infringing uses. Indeed, "substantial" is an understatement; there is no evidence that anyone has *ever* practiced these methods in the 40 years mifepristone has been used to treat Cushing's syndrome, the 11 years since Korlym was approved, or the four years since the Korlym label took its current form.

A physician can faithfully follow Teva's label and never infringe. Most obviously, if a physician administers mifepristone without co-administering a strong CYP3A inhibitor—i.e., just uses the drug for its FDA-approved indication—no infringement. If a physician administers

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infringing ones). This logical fallacy ran throughout Corcept's trial presentation. *E.g.*, Tr. 7:3–6 (Corcept Opening Statement) ("Dr. Snyder unequivocally testified that the instruction in Teva's label provide[s] 'a recommendation' to prescribe an infringing mifepristone dose *when co-administering*") (emphasis added); Tr. 223:24–224:10, 228:2–13 (Carroll) (Corcept's counsel asking Dr. Carroll what the label recommends "in instances where medical professionals determine that it is necessary to co-administer mifepristone and a strong CYP3A inhibitor"); Tr. 246:4–24 (similar); Tr. 349:23–350:16 ("THE COURT: So you're not arguing that this label induces someone to combine the two? MR. CERRITO: It doesn't need to …. THE COURT: What's encouraged? To co-administer the drugs? MR. CERRITO: *To dose-adjust when co-administering* ….") (emphasis added); Tr. 488:14–18 (Corcept's counsel asking Dr. Snyder whether, "*when prescribing mifepristone to a patient already being treated with a strong CYP3A inhibitor*, Teva's label instructs doctors to adjust mifepristone dose according to Section 2.5") (emphasis added).

a strong CYP3A inhibitor to a patient taking 300 mg or 600 mg of mifepristone and follows the label's titration instructions—no infringement. Tr. 271:19–272:17 (Carroll). And if a physician administers mifepristone to a patient already taking a strong CYP3A inhibitor and declines to titrate past 600 mg—no infringement. Tr. 268:5–12 (Carroll).

The presence of non-infringing uses, while not dispositive, is highly relevant. Even if "the defendant has actual knowledge that some users of its product may be infringing," courts are reluctant to infer intent to induce infringement "where [the] product has substantial noninfringing uses." *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1365 (Fed. Cir. 2003) (rejecting inducement argument where "fewer than 1 in 46 sales of th[e] product [were] for infringing uses"). This principle rests on sound common sense and applies with particular force here. Teva wishes to market its product with a label materially identical to the 2019 Korlym label. Tr. 15:22 Yet there is no evidence the 2019 label has led to *a single act* of infringement in four years. It is hardly plausible that Teva intends for its label to do what the identical Korlym label has not.

B. Binding precedent compels a finding of no inducement.

The Federal Circuit's decision in *HZNP* is directly on point and demonstrates that Corcept's inducement arguments fail as a matter of law. That case concerned a topical diclofenac sodium formulation indicated to treat osteoarthritis of the knee. The generic's label instructed patients to apply the formulation to their knee and further instructed to *"[w]ait until area is completely dry before covering with clothing or applying sunscreen, insect repellant, cosmetics, topical medications, or other substances*." *HZNP,* 940 F.3d at 700. The asserted patents claimed a method of (i) applying diclofenac sodium to the knee, (ii) waiting for the area to dry, and (iii) subsequently applying sunscreen or insect repellant to the treated area. *Id.* at 683, 700–02.

The district court granted summary judgment of no induced infringement because the label "*merely permits*, without encouraging, post-product application of sunscreen, insect

repellant, or a second topical medication." *Id.* at 686. The Federal Circuit affirmed, holding that the instructions in the label did not encourage application of sunscreen or insect repellant. *Id.* at 702. Instead, the relevant language was a "warning" that "operates in an 'if/then' manner: *if* the user wants to cover the treated area with clothing or apply another substance over it, *then* the patient should wait until the area is dry." *Id.* "This does not encourage infringement ...." *Id.*

The same reasoning applies here. Each asserted claim requires (i) co-administering mifepristone and a strong CYP3A inhibitor and (ii) adjusting the dose of mifepristone in a certain way. Teva's label does not encourage the co-administration step. Instead, it provides instructions about how to adjust the dose of mifepristone *if* the physician decides to co-administer. *See* Tr. 400:16–24 (Snyder). The expert testimony was unanimous on this point:

> Q. I have one section there highlighted under the main title subtitle, saying: 'Dose adjustment required.' What does that mean?
> A. That means that *if we're going to administer mifepristone together with a strong CYP3A inhibitor*, that you need to make an adjustment in the dose of mifepristone.

Tr. 217:19–24 (Carroll) (emphasis added).

> THE COURT: If you're going to co-administer, you must do this? Is that how you interpret that?
> THE WITNESS: That's how I would -- I think that's an even better interpretation.

Tr. 330:5–8 (Carroll).

> Q. What's the purpose of Section 2.5?
> A. The purpose is to warn physicians that there's an interaction between the two medications, and to do so only when necessary, and gives some recommendations as to how to adjust the dose *if the two were administered together*.

Tr. 399:4–8 (Snyder) (emphasis added).

Tellingly, Corcept's pre-trial brief relegates *HZNP*—by far the most factually on-point Federal Circuit precedent—to a footnote. *See* D.I. 270 at 23 n.4. And Corcept's attempt to deal

with *HZNP* in that footnote falls flat. Corcept asserts that *HZNP* "does not control a dispute such as this one, because the accused label instructs and requires each and every step of the claimed method (and provides no non-infringing alternative when treating a patient already receiving a strong CYP3A inhibitor)." *Id.*; *see also* Tr. 23:5–6 ("There are no optional steps here."). This assertion contains not one but two egregious misstatements.

First, Teva's label decidedly does *not* require "each and every step of the claimed method" because it does not require co-administration of mifepristone and strong CYP3A inhibitors. Indeed, Corcept has never even argued that the label requires co-administration.

Second, even in the event that a physician chooses to co-administer mifepristone and a strong CYP3A inhibitor, the label provides *multiple* non-infringing options of how to do so. For example, if a physician administers mifepristone to a patient already taking a strong CYP3A inhibitor, the label recommends beginning at 300 mg—a dose that would not infringe. Similarly, if a physician administers a strong CYP3A inhibitor to a patient taking 600 mg mifepristone, the label recommends reducing the dose of mifepristone to 300 mg—which would not infringe.

Corcept has also suggested that it can show inducement notwithstanding *HZNP* because co-administering mifepristone and strong CYP3A inhibitors will sometimes be "necessary," and the label describes infringing dosing adjustments for such cases. As an initial matter, Corcept has failed to prove that co-administering mifepristone and strong CYP3A inhibitors will ever be necessary. *Supra* Section I. Even setting that aside, *HZNP* considered and rejected that exact argument. There, the patentee argued that "application of sunscreen" was sometimes "medically necessary" and that, "when such need arises, [the label's] instruction will lead to an infringing use." 940 F.3d at 701. That, at most, established "the 'mere existence of direct infringement.'" *Id.* (quoting *Takeda*, 785 F.3d at 631). The label "merely provided guidance to patients about

what to do *if* the patient desired to have anything come into contact with the knee after application of the medication." *Id.* at 702. (emphasis added). This "if/then" language was insufficient: the label's instruction that "*if* the user wants to cover the treated area with clothing or apply another substance over it, *then* the patient should wait until the area is dry" did "not encourage infringement." *Id.* The same logic applies here.

Shire LLC v. Amneal Pharmaceuticals, LLC, is also instructive. No. 11-3781 (SRC), 2014 WL 2861430 (D.N.J. June 23, 2014), *rev'd in part on other grounds*, 802 F.3d 1301 (Fed. Cir. 2015). The claims covered a method of treating ADHD by administering a given drug product "with intake of food." 2014 WL 2861430, at *4. Amneal's generic label said "that the products may be taken 'with or without food.'" *Id.* at *5. The Court granted summary judgment of no induced infringement because "the statement that the medication may be taken with or without food cannot be reasonably understood to be an instruction to engage in an infringing use . . . . [I]t is indifferent to which option is selected." *Id.* At most, the court explained, the label "may be understood to permit an infringing use, but permission is different from encouragement." *Id.*

Teva's non-infringement position here is even stronger. Teva's label is not merely "indifferent" to whether a strong CYP3A inhibitor should be co-administered with mifepristone; instead, the label warns against such co-administration. If the indifference in *Shire* was insufficient for inducement liability, then the language in Teva's label must be as well.

C. Corcept's authorities are inapposite.

Corcept analogizes this case to the cases where courts have held that a defendant's label induced infringement. The stark differences illustrate why Teva is *not* liable for inducement.

1. In *Vanda*, the patent claimed a method of treating schizophrenia by (i) testing the patient to determine whether they were a CYP2D6 poor metabolizer and (ii) administering a

dosage of iloperidone to the patient of 12 mg/day or less for poor metabolizers and 12–24 mg/day for non-poor metabolizers. 887 F.3d at 1121. The defendant's label instructed physicians to administer "12 to 24 mg/day" iloperidone and stated that "the 'iloperidone dose should be *reduced by one-half* for poor metabolizers of CYP2D6.'" *Id.* at 1131. The label also states that "[l]aboratory tests are available to identify CYP2D6 PMs [poor metabolizers]." *Id.* The Federal Circuit held that "the district court did not clearly err in finding that [this language] 'recommends that practitioners perform or have performed a genotyping assay to determine whether patients are CYP2D6 poor metabolizers'" and then administer 12 mg/day or less for poor metabolizers and 12–24 mg/day for non-poor metabolizers. *Id.* at 1131–32 (citation omitted).

Thus, in *Vanda*, administering the product according to the approved indication led directly to infringement. Not so here. A prescriber administering mifepristone according to Teva's label may *never* co-administer a strong CYP3A inhibitor. Indeed, that is what the label recommends: physicians should avoid such co-administration if they can. And, even if co-administration occurs, it is possible to faithfully follow the label's instructions and not infringe.

2. In *AstraZeneca LP v. Apotex, Inc.*, (cited at Tr. 24:18–24), the patent claimed a method of administering a composition via nebulizer once per day. *See* 633 F.3d 1042 1046 (Fed. Cir. 2010). The generic label did not "explicit[ly] mention . . . once-daily administration" but instructed the patient to begin with two daily doses of 0.25 mg each and then "downward-titrate to the lowest effective dose once asthma stability is achieved." *Id.* at 1047, 1057. The Federal Circuit held that this language induced infringement because the downward-titration language necessarily instructed users to infringe: "the first step in titrating down from [0.25 twice daily] would have to be 0.25 mg once daily, as there was no way of decreasing the amount of each dose below 0.25 mg." *Id.* at 1057.

The instructions here—like the instructions in *HZNP* but unlike those in *AstraZeneca*—do not necessarily result in infringement. A physician following the label could easily choose never to administer a strong CYP3A inhibitor with mifepristone. For proof, one need look no further than the testimony here, where *both* sides' experts—who have 70 years of practice experience between them—have never done so. Tr. 266:9–23 (Carroll); Tr. 410:15–17 (Snyder); *see* Tr. 98:6–12 (Moraitis) (testifying that he had never co-administered the two drugs "because of the concerns for the potential interaction").

3. Corcept's reliance on *Janssen Pharmaceuticals, Inc. v. Mylan Laboratories Ltd.*, *see* Tr. 22:18–23:2, is also misplaced. There, it was undisputed that infringement would inevitably occur if physicians followed the generic label. The patent required a specific "reinitiation dosing regimen" of paliperidone for patients who were taking the drug but missed a dose. No. 20cv13103 (EP) (LDW), 2023 WL 3605733, at *7 (D.N.J. May 23, 2023). The label instructed how to reinitiate patients that missed a dose, and those instructions required clinicians to infringe when the patient returned between 4 and 9 months after a missed dose. *Id.* at *15. Uncontested evidence showed "that 'more than 50 percent' of [Janssen's] patients have missed a dose, including '20 to 30 percent' returning for an appointment 16 or more weeks (about 4 months) after the missed dose." *Id.* Thus, in the inevitable situation where a patient missed a dose and returned between 4 and 9 months later, the clinician had no choice but to infringe.

Here, by contrast, even if a physician decides to co-administer mifepristone and strong CYP3A inhibitors (which the physician would try to avoid in the first place) he or she could follow the instructions on the FDA label without ever infringing the asserted claims. Unlike in *Janssen*, there is no inevitable external occurrence that would require a physician following the label to infringe. Teva's label both discourages co-administration with strong CYP3A inhibitors

(and thus discourages infringement) and also offers non-infringing dosing options even to those who chose to co-administer despite the warnings (if anyone ever chooses to co-administer at all). Direct infringement can occur here only if the clinician assumes the risk of co-administering mifepristone and a strong CYP3A inhibitor *and chooses* to follow the particular label instructions that lead to infringement rather than the non-infringing instructions.

D. Corcept's "carve-out" argument is meritless.

Corcept suggested that the Court could infer specific intent because Teva did not attempt to carve anything out of its label. *See, e.g.*, Tr. 15:22–25, 19:24–20:4, 49:12–16. This argument fails because nothing in Teva's label induces infringement: the label does not encourage co-administration of mifepristone and a strong CYP3A inhibitor. There is nothing to carve out.[5]

More fundamentally, Corcept's arguments betray a misunderstanding of the legal standard for induced infringement. Corcept is required to show that Teva "took affirmative steps to induce." *Takeda*, 785 F.3d at 632 n.4. Its suggestion that Teva needed to take "affirmative steps to make sure others avoid infringement" "turns the legal test on its head." *Id.*; *cf.* Tr. 428:20–24 (Corcept's counsel suggesting incorrectly that Teva should have "ask[ed] the FDA for a label stating: Avoid co-administration of mifepristone and strong CYP3A inhibitors").

CONCLUSION

Teva respectfully requests that the Court enter judgment that Teva does not infringe the '214 and '800 patents.

[5] Corcept's argument is another attempt to jam this case into *AstraZeneca*'s inapposite mold. In *AstraZeneca*, the evidence showed that the defendant was "aware of the infringement problem presented by the proposed label" but "nonetheless proceeded with its plans to distribute its generic drug product." 633 F.3d at 1060; *see AstraZeneca LP v. Apotex, Inc.*, 623 F.Supp. 2d 615, 618 (D.N.J. 2009). Here, there is no evidence of any infringement problem, as stated above.

CONTAINS CONFIDENTIAL INFORMATION

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Respectfully submitted,

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